

LOSING MOMENTUM: ARE CHILDHOOD VACCINE SUPPLIES ADEQUATE?

HEARING BEFORE THE SUBCOMMITTEE ON PUBLIC HEALTH OF THE COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS UNITED STATES SENATE ONE HUNDRED SEVENTH CONGRESS SECOND SESSION ON

EXAMINING THE ADEQUACY OF CHILDHOOD VACCINE SUPPLIES, FOCUSING ON THE EXTENT THAT RECENT SHORTAGES HAVE AFFECTED IMMUNIZATION POLICY AND PROGRAMS, WHAT FACTORS HAVE CONTRIBUTED TO RECENT SHORTAGES, AND WHAT STRATEGIES ARE FEDERAL AGENCIES CONSIDERING TO HELP MITIGATE THE DISRUPTIONS IN SUPPLY

SEPTEMBER 17, 2002

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LOSING MOMENTUM: ARE CHILDHOOD VACCINE SUPPLIES ADEQUATE?

TUESDAY, SEPTEMBER 17, 2002

U.S. SENATE,
SUBCOMMITTEE ON PUBLIC HEALTH,
OF THE COMMITTEE ON HEALTH, EDUCATION, LABOR, AND
PENSIONS,
Washington, DC.

The subcommittee met, pursuant to notice, at 2:34 p.m., in room SD-430, Dirksen Senate Office Building, Senator Reed, presiding.
Present: Senators Reed and Murray.

OPENING STATEMENT OF SENATOR REED

Senator REED [presiding]. Let me call the hearing to order.

Good afternoon. Today's hearing will examine a critical issue for the health of our Nation—the stability and adequacy of our childhood vaccine supply.

Indeed, shortages of 8 of the 11 recommended childhood vaccines have plagued our health care system for the past 12 to 18 months and have affected every segment of our society. We will hear today that too many children are going without timely vaccinations. Physicians have been forced to turn away young patients. State and local public health officials have been left scrambling for vaccine supplies, and school departments have had to waive immunization requirements for entry, leaving young children vulnerable to potentially devastating, yet entirely preventable, diseases such as measles, rubella, and even chicken pox.

Last year, I had the opportunity to chair a hearing of the HELP Committee that explored some of these issues. Since then, several members of this committee and others concerned about the critical shortage of vaccines commissioned a report by the General Accounting Office to get a better handle on the root causes for the recent shortage.

It is clear from this report that we have a system that cannot guarantee an adequate supply of vaccines from year to year and is unprepared to handle a potential outbreak of many routine childhood diseases. We are putting our children in danger. Congress, the administration, medical providers and manufacturers must work together to ensure an adequate and reliable supply of vaccines.

Vaccines are one of the greatest public health accomplishments of the 20th century, reducing once common diseases by 95 to 99 percent. Yet the campaign to protect our Nation's children from the

ravages of these contagions has in many ways been the victim of its own success. Today, most parents have never heard of these diseases, except when they bring their children in for well-baby visits, and providers have limited experience actually treating them in the practice setting.

In addition, significant consolidation in the vaccine manufacturing industry over the past two decades has resulted in a decline in the number of producers in the market. Over a dozen manufacturers existed prior to 1980. Today, only four manufacturers produce almost all of the routine childhood vaccines on the United States market.

The GAO report outlines the factors that contributed to the recent shortages and paints a disturbing picture for the future of our vaccine supply. We are clearly at a point where swift action must be taken to preserve and strengthen our immunization system.

I am particularly concerned that the recent vaccine supply disruptions will inevitably have a negative impact on vaccine coverage rates in this country. The public health community must remain vigilant in tracking this data so that the appropriate response can be taken to protect public health.

We simply cannot allow decades of tremendous progress in reducing vaccine-preventable diseases to become undone.

In addition to Jan Heinrich of the GAO, also testifying before the subcommittee today are Dr. Timothy Doran, a physician from Baltimore and a member of the American Academy of Pediatrics, and Wayne Pisano, of Aventis Pasteur, one of the four remaining vaccine manufacturers in the United States market.

I look forward to hearing each of your perspectives on the recent vaccine shortages and your reactions to the findings and recommendations articulated by the GAO.

I would like to thank all of our witnesses for taking the time to be here today to discuss this important issue, one which affects each and every one of us.

Now, as my colleagues arrive, I will recognize them, but Ms. Heinrich, please go ahead.

STATEMENT OF JANET HEINRICH, DIRECTOR, HEALTH CARE-PUBLIC HEALTH ISSUES, U.S. GENERAL ACCOUNTING OFFICE, WASHINGTON, DC

Ms. HEINRICH. Mr. Chairman, we are pleased to be here this afternoon to discuss findings from a report which we are releasing today that you and several others in Congress requested on the recent incidents of vaccine shortages.

Immunizations, as you said, are considered one of the leading public health achievements of the 20th century. Immunization programs have eradicated polio and smallpox in the United States and much of the world and reduced the number of deaths from several childhood diseases, such as measles, to near zero.

A consistent supply of many different vaccines is needed to support this effort. The Centers for Disease Control and Prevention recommends that routine immunizations be given against 11 childhood diseases, four of which were added to the schedule in the last 10 years.

The recent incidents of vaccine shortages began in the fall of 2000 when supplies of the tetanus and diphtheria booster fell short. As you can see on this chart, supplies of other vaccines also declined, and by fall 2001, CDC reported shortages of five vaccines that protect against eight childhood diseases.

Recent reports suggest that most supplies are now beginning to return to normal.

In response to these shortages, State immunization programs rationed the amount of vaccines distributed to providers and recommended deferred immunizations for some children so that available supply could be directed to those at highest risk. Many States also suspended immunization requirements, allowing children to attend day care and school with fewer of the previously recommended vaccinations.

No single reason explains the recent shortages. Rather, multiple factors coincided that affected both the supply and the demand for vaccines. We identified four key factors—problems in the manufacturing process due to several factors, including changes to assure compliance with good manufacturing practices; the removal of thimerosal from vaccines; manufacturers' sudden decision to discontinue production; and unanticipated demand for new product.

Manufacturing and production problems such as slowdowns or plant maintenance activities taking a bit longer than expected contributed to the shortage of several vaccines. Changes over the last several years in FDA inspection practices may have resulted in the identification of more or different instances of manufacturers' non-compliance with good manufacturing practices. These inspection program changes were not well-communicated by FDA to manufacturers.

As a precautionary measure, in July of 1999, the American Academy of Pediatrics and the U.S. Public Health Service issued a joint statement advising that thimerosal, a mercury compound used as a preservative in vaccines, be eliminated or reduced as soon as possible. Efforts to remove thimerosal affected the production of several vaccines and contributed in particular to the shortages of DTaP. Removing the preservative was complex, and for some manufacturers just not possible.

Another major factor in the shortage of DTaP and tetanus toxoid was the decision of one manufacturer to discontinue production of all products containing tetanus toxoid. This company experienced difficulties removing thimerosal from its vaccine and also in responding to a consent decree requiring significant upgrades in its facilities involved in producing tetanus toxoid. The manufacturer had produced approximately one-quarter of the tetanus toxoid and about one-quarter to one-third of all DTaP distributed in the United States.

A new pneumococcal conjugate vaccine was added to the recommended schedule in January of 2001 and was accompanied by an extensive education campaign by the company prior to its availability. The company was only able to provide about half the needed doses during the first part of 2002, and the demand continues to outstrip the supply.

While the recent shortages have been largely resolved, the vaccine supply remains vulnerable to disruptions that could occur in

the future. Although there may be some excess manufacturing capacity, the production of vaccines is a lengthy process and prevents the quick production of more vaccine when disruptions occur.

The limited number of manufacturers poses another problem. Five of the eight childhood vaccines have only one company producing the vaccine for the U.S. market. Several new formulations under development, once approved by FDA, could reduce the number of sole source vaccines.

In conclusion, Federal efforts to strengthen the vaccine supply have taken on greater urgency with the recent incidents of shortages. The Federal role in the supply and demand of vaccines is extensive, including the development of the schedule, the purchase of over 50 percent of the childhood vaccines administered in the United States each year, and the regulatory oversight to ensure safety, efficacy, and compliance with good manufacturing practices.

Several strategies for strengthening the supply are being put forward. While many of these hold promise, ensuring an adequate supply for the future poses continuing challenges.

Mr. Chairman, this concludes my remarks, and I am happy to answer any questions.

[The prepared statement of Ms. Heinrich may be found in additional material.]

Senator REED. Thank you very much.

I should point out that not only being director of the health care group at the U.S. General Accounting Office, Dr. Heinrich has an extensive resume—she is a graduate of the University of Michigan School of Nursing and a master's of public health from Johns Hopkins University. This experience is quite evident not only in your report but in your presentation. So thank you very much, Dr. Heinrich.

Let me ask a question or two. One of the aspects of the GAO report is the indication that vaccine stockpiles are considered to be a potential short-term strategy that could help mitigate crises. The report also goes on to note that supply at least the CDC has the authority under the National Vaccine Program as well as the Vaccines for Children Program to stockpile. Yet, only two vaccines are currently stockpiled, and we are uncertain as to how many doses are there—they are the MMR and the IPV.

To me, this underscores the very basic issue, of how do we urge HHS to develop a strategy uniting all the disparate elements—CDC, FDA, manufacturers, health care providers—to deal with not only the stockpile issue but also the other issues we discussed. HHS—and you might comment—is in the best position to put this strategy in place. Without this strategy, we will continue to deal with some symptoms of the issues but not the whole, systemic cause of the vaccine shortages.

Could you elaborate, Dr. Heinrich?

Ms. HEINRICH. The National Vaccine Policy Office is charged with coordination of all the different elements of the Department of Health and Human Services that are involved in policies related to vaccines, both in terms of the supply, demand, and the regulatory safety issues.

They are also charged with including the other important stakeholders, that being States as well as the manufacturers.

I think there are questions about how effective the National Vaccine Program Office has been able to be. They have recently moved the office from CDC to the office of the Assistant Secretary for Health, but we know that there has been limited funding, for example, in the past.

Certainly in terms of stockpiling, we say in our report that the authority that CDC has to stockpile is clear for the program for vaccines for children. That program has eligibility requirements, so it does not cover all children, so there is a need, we feel, for clarification of the authority that CDC has to stockpile.

In terms of your question on overall strategy, we feel that that is absolutely critical, and we then outline many components of that strategy that have to be thought about, everything from how much and in what form it is stored, who stores it. Currently, the two vaccines that are stockpiled are stored by the manufacturer, and that vaccine is rotated through their ongoing inventory so there is always an updated supply. So do not think of it as just sitting on a shelf; it is vaccine that is in constant rotation.

But if a stockpile is going to be effective, there has to be that strategic perspective that you note.

Senator REED. And just for the record, your view would be that HHS is the appropriate agency to develop this strategic approach?

Ms. HEINRICH. Yes, certainly, we do think it is HHS, because other than, for example, the Department of Defense, which has other needs, it is the Department of Health and Human Services that is responsible.

Senator REED. Again, I appreciate your insights and comments, and if there are other things that you feel the Congress should do—and from your response to questions, to clarify some of the authority of CDC and ensure that the Office of Vaccine Policy is funded and robustly supported are the two principal recommendations—is that correct?

Ms. HEINRICH. Those certainly are important. We also make recommendations that focus on the role of the Food and Drug Administration because, as we have said, those vaccines that are in the review process have the potential to alleviate some of the stress in the system in terms of having other manufacturers supplying some of the recommended vaccines for children.

The FDA does have procedures that they could use to expedite the review of these vaccines. It is their current policy that vaccines that are currently used in the market do not qualify for this expedited review, and we are suggesting that they look at that policy because they could in fact find that when we have supplies that are fragile, that is enough rationale for the expedited review of those vaccines that could add available products for children's vaccines.

Senator REED. Thank you.

I understand that several of the childhood vaccines are price-capped under Federal purchase contracts. Did you find that these price caps played a direct role in causing any of the recent shortages?

Ms. HEINRICH. We certainly did not find that they played a direct role, and that is because some of the vaccines that are capped were not in short supply. Some of the more recent vaccines that cost

more and are not under caps were in short supply. The only vaccine that is at the cap that was in short supply was MMR.

Senator REED. Thank you.

The report also talks about the Vaccine Injury Compensation Program, and offers some recommendations to streamline it to make it more effective. However, I would note on page 8 of your testimony that the working group did not conclude that this program was a cause of any of the shortages. Is that accurate?

Ms. HEINRICH. Certainly in the data that we obtained, we did not hear people saying that this shortage that we have just experienced was directly linked to the problems and concerns about vaccine liability. However, we certainly did hear from manufacturers that it is a growing problem, and we certainly did check into the Vaccine Injury Compensation Program to see what claims they have received, and we did find out that there are over 800 claims that have been added to the Vaccine Injury Compensation program, many of them related to the thimerosal and removal of thimerosal issues.

Senator REED. Let me ask you a final question before I recognize Senator Murray for her opening comments any questions.

Among the several areas of concern is the manufacturing capacity. I think you have commented on the FDA's role in ensuring that capacity. Is there a consideration for some type of Government-owned or operated company? I know some of these private companies have very checkered histories, but have you considered that at all in your review?

Ms. HEINRICH. Certainly when we were talking with people and collecting data, we asked them what they thought of the proposal for a Government-owned program and also checked with an organization in Massachusetts that is a Government-sponsored manufacturer of DTaP and tetanus, as a matter of fact. Our conclusion is that, one, not too many people that we were talking with advocated this, but second, the Government-owned facility would be under the same regulatory processes and procedures that the private sector is and would have the same challenges in meeting those good manufacturing practices.

We also heard that having a Government-owned facility, certainly where there are viable products in the market, would be a rather chilling effect to the private sector.

Senator REED. Thank you very much, Dr. Heinrich.

Senator Murray?

Senator MURRAY. Mr. Chairman, thank you very much for having this really important hearing. I appreciate it, and I certainly appreciate Ms. Heinrich's testimony and her being here today as well.

There has been a lot of speculation about the delays and shortages, and I think this report gives us a much better basis for understanding what the scope of the problem was and what happened, and I think it is not because of one specific thing, but a number of things happened that together over the last 3 years created this problem, and I hope that all of us will look at ways that we can provide a better infrastructure in the future so we do not have these kinds of delays.

In my State, I was hearing from a lot of different sectors, certainly from schools, which require immunizations before they allow kids to come in, and kids were coming in and saying, "I cannot get them"; obviously, from pediatricians and public health officials, who were really concerned because they were not getting their supplies on time; and lots of other people.

So I am glad that we are now hearing that there is no shortage particularly right now, although in my State, we are still hearing that there is a problem with some of the catch-up kids who did not get their immunizations on time and are now trying to go back and get them and get back in line, and I think that is going to cause us some problems for a while that we need to address.

So Mr. Chairman, I really appreciate this opportunity, and I just have a few questions that I wanted to ask Ms. Heinrich while she is here today.

Your report indicates that vaccine shortages have peaked, and most supplies are returning to normal. I wanted to know how you documented that. Do you collect data from State and local health officials? Are they private providers or physicians' offices? How do you calculate that?

Ms. HEINRICH. Certainly the work that we did and reflected in the report was on our survey of States. In terms of there being a supply that is available now, we obtained that information from the Centers for Disease Control and Prevention.

It should be noted that although CDC is saying that overall, there are adequate supplies, they footnote that there is not enough for aggressive catch-up campaigns as you suggested. It is also very clear that the pneumococcal conjugate, the PVC, is still in short supply.

Senator MURRAY. The reason I ask is because I am still hearing from some parts of my State that there is a shortage, so I am just wondering who CDC is asking in order to get the information back to you that the problem has been solved.

Ms. HEINRICH. They would be in contact with those State immunization programs. And I think that to understand what the private sector is experiencing, we would need to go to organizations such as the American Academy of Pediatrics.

Senator MURRAY. Did you do that in your report?

Ms. HEINRICH. We did not.

Senator MURRAY. OK. In reviewing the data on the impact of the shortages, did you find any particular increases in the reported cases of some of the childhood illnesses, like measles?

Ms. HEINRICH. We actually looked very aggressively to see if there would be any evidence of increased infectious diseases as a result of the delay in children obtaining these immunizations. We could not find any evidence.

On the other hand, there will always be a lag time in terms of the reporting of those infectious diseases, so we may not know about this for another period of time, even up to a year.

Senator MURRAY. The other question I have is why there are such discrepancies in the number of vaccines in short supply and why some States and local public health offices experienced longer and more supply distractions. It appears in your report that 52 of the programs experienced shortages of two or more vaccines, but 31

of the programs reported shortages of five or more vaccines, and nine programs had shortages of one or more vaccines for 12 months or longer. Is that a matter of population? Are there other factors that contribute to these kinds of discrepancies that you report?

Ms. HEINRICH. Each State has its own immunization program and its own policies and procedures and its own ability to buy and stockpile vaccines. So part of what you are seeing is that each State is unique in terms of what stockpiles they might have had.

What happens is that CDC gives grants to States under their 317 Program. The States can then purchase vaccines through that program and through State moneys, as a matter of fact, if they so choose. Then, it really is again up to the State policy in terms of whom they distribute that to, who participates in their program. Oftentimes, you will have private sector as well as public sector providers involved.

Senator MURRAY. I appreciate your input on that. Thank you.

Thank you, Mr. Chairman.

Senator REED. Thank you very much, Senator Murray.

Again, Dr. Heinrich, thank you so much for your testimony and for your excellent report.

Ms. HEINRICH. Thank you.

Senator REED. Let me now call the second panel to the witness table.

We are joined today by Dr. Timothy F. Doran. Dr. Doran lives in Baltimore, MD. He has been a practicing pediatrician for nearly 20 years, and has chaired the Department of Pediatrics at the Greater Baltimore Medical Center in Baltimore since 1999. Dr. Doran received his Bachelor of Arts degree from Harvard College, in Cambridge, MA, and his medical degree from Tufts University School of Medicine in Boston. He completed his pediatric residency at Montefiore Hospital and Medical Center, the Bronx, NY, and was chief resident at the Albert Einstein School of Medicine's Department of Pediatrics at Montefiore.

Dr. Doran served as president of the Maryland Chapter of the American Academy of Pediatrics from 1996 to 1998 and was honored as Pediatrician of the Year by the Maryland Chapter in 1998. Dr. Doran is the current chairman of the AAP's National Nominating Committee.

In addition to his work at the State and national levels for the American Academy of Pediatrics, Dr. Doran has held numerous board and committee positions advocating for underserved populations of children, including victims of sexual abuse and children with disabilities and other special health care needs.

Dr. Doran is married and has two children.

I want to thank you for being here. Dr. Doran also grew up in North Attleboro, MA, which is almost as good as being in Rhode Island, and his father worked in Rhode Island, so that makes up for it. We welcome you particularly, Dr. Doran.

Wayne F. Pisano, our next witness, is the executive vice president for Aventis Pasteur North America. He has overall responsibility for both the United States and Canadian businesses. Additionally, he serves as the head of the global market process team and chairs several North American executive committees.

Mr. Pisano joined Aventis Pasteur in 1997 as vice president of marketing and was promoted to senior vice president of marketing and sales during April of 1998. Mr. Pisano has played a strategic role in resolving vaccine supply issues and recommending approaches to prevent recurrences.

Mr. Pisano holds a bachelor's degree in biology from St. John Fisher College and a master's degree in marketing from the University of Dayton.

Thank you both for joining us. Let me ask Dr. Doran if he would proceed. Your testimony will be made a part of the record by unanimous consent. If you would like to abbreviate it or summarize, that would be accepted and appreciated.

Dr. Doran?

STATEMENTS OF DR. TIMOTHY F. DORAN, CHAIRMAN OF PEDIATRICS, GREATER BALTIMORE MEDICAL CENTER, BALTIMORE, MD, ON BEHALF OF THE AMERICAN ACADEMY OF PEDIATRICS; AND WAYNE F. PISANO, EXECUTIVE VICE PRESIDENT, AVENTIS PASTEUR NORTH AMERICA, SWIFTWATER, PA

Dr. DORAN. Thank you, Senator.

Good afternoon, Mr. Chairman and Senator Murray. As you mentioned, I am Dr. Tim Doran, a practicing pediatrician and chairman of pediatrics at Greater Baltimore Medical Center, a community hospital in Baltimore, MD.

On behalf of the American Academy of Pediatrics, I thank you for the opportunity to testify today about the current shortage of childhood vaccines.

My practice consists of about 1,800 children from predominantly middle-class families. In the past, however, I practiced in many different locales, from a poor island in the West Indies to inner-city Baltimore.

In the 20 years that I have been practicing, I have never experienced the severe shortage of required immunizations as I have in the past year.

This afternoon, I want to address three key points. First, I will describe the consequences of the vaccine shortage to patients and their families. Second, I will tell you about the administrative impact on pediatric practices. And finally, I will summarize the American Academy of Pediatrics' recommendations to address this problem.

The heart and soul of a pediatrician's job is disease prevention. The predictable delivery of safe and effective vaccines is central to our goal of keeping children healthy. In recent months, my practice has seen shortages in several routinely-administered vaccines, as you have heard, reflecting a national trend. In fact, just last week, I again ran out of the new pneumococcal vaccine, Prevnar. This vaccine protects children from life-threatening meningitis, pneumonia, and blood infections.

A pediatrician from New Mexico reported that his high-risk population of American Indian infants is also currently out of this vaccine. This is especially troublesome because this past spring, he diagnosed a 4-1/2-month-old Navajo infant with a case of pneumo-

coccal meningitis—a vaccine-preventable and potentially fatal childhood illness.

The parents of my patients have been understandably anxious when they learn that a vaccine is unavailable. They know that there is a small but finite chance that their child might become ill with an otherwise easily preventable illness because of a delayed or missed vaccine.

Because of media coverage of anti-vaccine groups, I spend a significant amount of time with many parents, reassuring them that our vaccines are safe and beneficial. I cannot help but wonder how my credibility and that of my colleagues suffers when I then have to explain that these important vaccines are not available for their child.

In addition to the major risks to patients and worry to parents, the vaccine shortage has had an administrative impact on my practice as well. We must now create a system of callback lists to reach those most in need of missed vaccines when they become available. Our experience has been that these systems are not very reliable or effective. Even if my relatively affluent practice, the level of compliance with these callbacks is far from perfect and clearly inferior to immunizing at routine checkups.

I have also had to explore creative and time-consuming alternative methods to procure the full supply of vaccine that my practice needs. It is another reminder to me of the lack of a coordinated distribution system that has led to spotty supplies.

At the same time as the shortages of 8 of the 11 required vaccines occurred, one vaccine for older adolescents and adults to prevent Lyme disease was pulled from the market because it was unprofitable. Although this was not a required immunization, its disappearance reminds pediatricians that vaccine decisions can sometimes be driven more by economics than by public health considerations.

The bottom line is that the public requires a secure supply of all the recommended pediatric vaccines, vaccines that save children's lives and are the most cost-beneficial medical intervention in history.

We must safeguard our children from preventable interruptions in vaccine delivery. This should never happen again in this country.

One immediate step is necessary. The Federal Government should provide and adequately fund the creation of stockpiles, as mentioned, for all recommended vaccines, stockpiles of sufficient size to ensure that significant and unexpected interruptions in manufacturing do not result in shortages for children.

The GAO report recognizes and the Academy supports the importance of this stockpile for childhood vaccines, including the development of a comprehensive strategic plan to implement the vaccine stockpile.

Another crucial step is to preserve and strengthen the liability protection for consumers, manufacturers, and physicians through the Vaccine Injury Compensation Program. The VICP has become an integral part of maintaining the vaccine market. Enacted in the late 1980's with the support and guidance of the American Academy of Pediatrics, the VICP has helped to stabilize what was then

and appears again to be a fragile vaccine market. We reiterate our strong support that claims for vaccine-related injury or death must be filed first with the VICP. We appreciate the efforts by Dr. Frist and others to craft modifications as necessary to ensure that the VICP is working to its full potential.

The American Academy of Pediatrics participates in the work of the National Vaccine Advisory Commission. The recommendations of NVAC, coupled with some of the other GAO recommendations, create an excellent starting point to address a system that must be fixed.

Universal immunization is a fundamental public health measure that has profoundly improved the health of our Nation. It would be tragic to let this hard-won advance slip away. The health of our children depends on it.

Thank you for your time and attention.

Senator REED. Thank you very much, Doctor.

[The prepared statement of Dr. Doran may be found in additional material.]

Senator REED. Mr. Pisano?

Mr. PISANO. Mr. Chairman, Senator Murray, good afternoon.

I am Wayne Pisano. I am the executive vice president for Aventis Pasteur North America, and I would like to thank the committee for providing us this opportunity to offer input on issues that are so vital to the health of our Nation.

Aventis Pasteur is one of the leading developers and manufacturers of vaccines, with U.S. headquarters in Swiftwater, PA. Vaccines have been produced at Swiftwater, PA since 1897.

Aventis Pasteur is one of four global vaccine companies supplying pediatric vaccines in the United States. Many people are surprised that the industry is so small, but that is a direct result of the 1980's liability crisis that drove many companies out of the market.

We have in this country a unique and amazing vaccine enterprise that has resulted in freedom from disease for millions of children. Many physicians would be treating some tens of thousands of cases of rubella, diphtheria, pertussis, and other potential killers if not for our successful efforts. Vaccines in the hands of a robust, cooperative public and private health delivery system have made these diseases historical artifacts.

The country is now emerging from an 18-month period during which there were a number of vaccine shortages. Today I am pleased to report that there is ample tetanus vaccine for all needs, and there is ample pertussis vaccine. It is our understanding that supplies of varicella and MMR vaccine are returning to normal.

In the face of numerous factors, the fact that the private sector can and has responded to supply issues demonstrates its underlying strength and vitality. Having said that, we need to establish a national policy addressing how best to prevent or minimize the likelihood of recurrences. Our company offered a series of recommendations earlier this year. This hearing offers an excellent opportunity to discuss these with this committee.

While my full testimony provides a more comprehensive look at the vaccine enterprise, including the underlying causes of the re-

cent shortages as well as the additional threats in the future, the basics can be succinctly stated.

First, vaccines are extremely difficult to produce. I said there were only for global manufacturers of pediatric vaccines in the United States, and some of these are single-source providers. If one of the manufacturers unexpectedly experiences production difficulties or leaves the market, it can cause supply disruption.

Second, the lengthy and costly process of new product development combined with time-consuming production cycles adds up to a complex regulatory process that discourages new entrants.

Third, despite their undisputed value, vaccines historically have been extremely low or commodity-priced. Federal programs that cap vaccine prices may produce short-term savings for the Government but ultimately contribute to the supply problem. If return on a manufacturer's investment is unacceptably low, that business cannot survive.

Fourth, as some members of this committee will recall, the liability crisis of the 1980's drove many manufacturers out of the market. We are today facing liability problems that dwarf what we saw two decades ago, which potentially pose a threat for future supplies.

I would like to talk about what can be done to improve the immunization enterprise, effectively presenting a vaccine supply agenda for your consideration.

We have offered a number of legislative and policy proposals during the past year that we believe will provide a tune-up for the system and a coherent approach for the long-term stability. These proposals are consistent with both the GAO report and the draft recommendations now under review by Secretary Thompson's National Vaccine Advisory Committee.

First, it is time to seriously consider building a strategic vaccine reserve by creating stockpiles for use if supplies are disrupted. Had this been the case when one company recently discontinued tetanus vaccine production, a shortage would have been unlikely.

Second, manufacturers should voluntarily pledge to provide advance notice if they plan to cease production. Several months ago, Aventis Pasteur publicly pledged to give at least 6 months of notification before discontinuing any production. We believe that this pledge, as with other good business practices, need not be legislated. We understand that a bipartisan group of Senators on this committee is attempting to shape an appropriate advance notice provision. We look forward to working with you on this issue.

Third, we urge you to reform the Vaccine Injury Compensation Program in two ways. It can and needs to be made more family-friendly, and second, we need to reaffirm the original intent of the Vaccine Injury Compensation Program so that all vaccine claims initially proceed through the program.

My full testimony outlines in some depth the creative ways in which the law you enacted in the 1980's is being circumvented. In an industry with total U.S. revenues of \$2.5 to \$3 billion, Aventis Pasteur alone faces over 100 lawsuits, with more being filed every week, that seek far beyond this amount in damages. Tease cases should be moved back to the Vaccine Injury Compensation Program as Congress intended.

We support Senator Frist's bill, S. 2053, which accomplishes the twin goal of making the program more family-friendly for claimants while bringing such claims back within the Vaccine Injury Compensation Program. We are now spending millions of dollars defending against these suits, suits in which we believe we will ultimately prevail but at an enormous cost to the viability of the industry and to the immunization enterprise.

Frankly, the liability issue dwarfs all others as a threat to the stability of the vaccine supply, and we urge you to pass this bill before you adjourn.

Fourth, FDA funding in the area of vaccine testing research needs to be increased. Budget cuts in recent years threatened FDA's competency in this important area. With CBER currently undergoing organizational changes, the time is right for restoration of these resources.

There are also a number of nonlegislative actions that can have real and lasting impact on vaccine supply. For example, we have urged that the CDC be encouraged to act on confidential information in ways that can provide for managing and stimulating alternative supply to minimize shortages. We believe that the CDC can act under its current authority as a confidential facilitator of critical supply information with the manufacturer's permission.

Other nonlegislative initiatives include adequate reimbursement to providers for immunization services. This is also outlined in my written testimony.

Several proposals in Congress would actually undermine incentives for manufacturers to produce vaccines. Whether called the National Vaccine Authority, a GOCO or a GOGO, each of these proposals results in the Federal Government getting into the business of manufacturing vaccines. We do not believe that any of these approaches would be constructive measures for addressing supply issues.

The vaccine enterprise in this country is a remarkable success story. I do not believe that it is fragile at its core, but it clearly has several areas that can be strengthened.

Thank you for your attention and your commitment to the immunization system in this country.

[The prepared statement of Mr. Pisano may be found in additional material.]

Senator REED. Thank you very much, Mr. Pisano, for your testimony. Thank you both for excellent testimony.

Let me proceed to questions. Dr. Doran, the GAO report suggests that there are a number of vaccines under development which could mitigate potential shortages in the future, but often, these new vaccines are very expensive—the PCV, the pneumococcal vaccine, is an example of a rather expensive vaccine.

Do you anticipate the cost of these new vaccines as a potential barrier to access to immunization?

Dr. DORAN. The barrier certainly comes in terms of the number of vaccines given versus the cost, and obviously, most pediatricians will opt for whatever is the most convenient and most effective vaccine strategy, and most pediatricians will abide by the ACIP and the CDC recommendations, and the financing is not generally the major consideration.

The liability issues are serious. Influenza vaccine is now on the docket in terms of 24-month-olds. It is not currently covered under the VICP, so pediatricians from a personal liability standpoint have some trepidation going forward unless there is clear coverage from the liability standpoint.

Senator REED. Thank you.

Let me follow up with another question on an issue that you alluded to in your testimony. There is the administrative disruption of calling children back and determining who has missed a vaccination. I fear it might lead to what is really a lost generation of children who have missed their routine vaccine, they have moved, or you cannot get them back, and we now have a cohort of unvaccinated children because of these shortages.

How are you and your colleagues trying to manage to avoid that lost generation?

Dr. DORAN. The majority of the immunizations that we give are in the first 2 years of life. There are a number of regular, routine visits, and any pediatrician or family practitioner or someone delivering health care to children should be checking their vaccination records. In terms of losing them over years, I do not anticipate that that would be a problem. The fear for pediatricians is if you have missed the first couple of doses, and the child comes down with a preventable illness.

But the problem is there, and I think we will just have to see how much of a problem from those lost vaccinations over this period of time, how effective we are at recapturing those children. My anticipation is that there is adequate room in terms of the periodicity schedule of when children come to see physicians that it can be rectified. However, I think your point is well-taken.

Senator REED. Thank you very much.

Mr. Pisano, you and Dr. Doran and the GAO conclude that there is merit in some kind of stockpiling, but the GAO report identifies some key questions, and I wonder how industry can help answer questions like, for example, what quantity to stockpile, the form and storage of stockpiled vaccines, insuring that vaccine quantities are in addition to normal supplies.

Can you give us a response to these questions? I know you are speaking in behalf of your company, but could you give an indication of potential industry response and also, obviously, ongoing cooperation on this matter?

Mr. PISANO. I think the current guidelines recommend a 6-month stockpile for the VFC program. This is what CDC has authorized to do and obviously, as has been pointed out, we are not quite there.

We would actually recommend that NVPO form working groups with CDC, FDA, and the vaccine manufacturers to address each individual vaccine. In some cases, we have multiple manufacturers; in some cases, we have single manufacturers; in some cases, we have second vaccines in the development process such that there will be a second manufacturer in the future. I think each vaccine ought to be looked at individually to determine how much vaccine should be in a safety reserve, who should do that in terms of which manufacturer or multiple manufacturers. And in fact, there are other vaccines that potentially could actually be kept at bulk level

and not into finished goods, and you may have a longer shelf life than I think was earlier recognized. There is a shelf life, and the current stockpile have to be rotated because of the expiration date on the production lots.

Senator REED. Thank you, Mr. Pisano.

Aventis Pasteur has publicly stated its support for a notification requirement. Let me commend you for that. I think that is a sensible approach. And the GAO report indicates that no manufacturer would object to a 6-month notice requirement similar to what they do now for other drugs.

What kind of notification requirement do you think all the manufacturers could agree on, and what would it look like in practice? Would it be 6 months? Would it be longer? Could you give us any indication?

Mr. PISANO. It is difficult for me to speak on behalf of the other manufacturers, and I think that is something that it would be worthwhile hearing from them on. Aventis Pasteur believes that a minimum of 6 months would be necessary. We also see that linked into the stockpile, so there is basically a safety reserve there.

In terms of the need to legislate versus volunteering pledges, I think that is something that the committee needs to discuss further.

Senator REED. Good.

Both of you and the GAO report have concluded that two of the major responses to this shortage would be a notice requirement to at least let the market and all the providers know if a manufacturer is going off line, and also some type of stockpile.

Is there another major recommendation that you would add to those two?

I will ask you, Mr. Pisano, and then you, Dr. Doran.

Mr. PISANO. I think it is important for the CDC to be able to share confidential information as well as work collaboratively with the FDA. There are times when the Government policymakers know that there is a potential problem or a problem occurring with one manufacturer. If they have the ability to notify the other manufacturers at that time, we can adjust manufacturing production schedules.

I think a good example of that was 2 years ago with influenza, when one manufacturer left the marketplace, and another was experiencing significant difficulties in manufacturing. Had CDC notified the other manufacturers, we could have adjusted production schedules. It would not have totally eliminated the problem, but it would have basically reduced the magnitude that this country experienced.

So we need the CDC to share this information in the best interest of the immunization enterprise.

Senator REED. Thank you, Mr. Pisano.

Dr. Doran?

Dr. DORAN. The additional items that I would include would be the liability issues that we discussed, but also the administration fee for providers. It was proposed to reduce the administration fee for pediatricians to a level where they would actually be losing money with each vaccination. That is in discussion right now, is my understanding, with CMS and stakeholders in that, and they are

hopefully arriving at a suitable solution to that, but the original proposal was to make the administration fee so low as to be prohibitive to providers.

I spend a tremendous amount of time with parents explaining about the issues of MMR and autism, of thimerosal. It is an enormous undertaking in terms of my time. So the administration fee needs to be commensurate with the time and effort and syringes and storage and all those other factors. So that is something that needs to be on the radar screen as well.

Senator REED. I know there are some who propose or suggest that to support the reduction that many times, nurses administer these vaccines. But your point would be that that is in cooperation with the physician who spends other time explaining and counseling; is that fair?

Dr. DORAN. Senator Reed, I have many lawyer parents, and they do not want a 20-second answer on the relationship of MMR and autism. These are discussions that can be prolonged, and you cannot walk out of the room and say, "I cannot answer that. You just have to get your vaccine."

So these are serious matters and would impact; if the reductions were made, I would predict they would have a serious adverse impact on the whole immunization program.

Senator REED. Let me ask a final question. I think this has been an excellent hearing, beginning with an excellent report from GAO which was very substantive and very thorough. Both of your testimony has been on point and very helpful. I will give you an opportunity to look ahead into the future. What do you believe is the greatest challenge to the vaccination program, either something that we have discussed or that we might not have touched on?

Mr. Pisano?

Mr. PISANO. I think the liability issues that we are facing going forward really dwarf anything we have ever faced before. I think it is critical that the Vaccine Compensation Program be strengthened, be made more family-friendly. Clearly, there are enough complaints from parents that it is problematic getting through the system and needs to be reexamined. And we need to make sure that when problems occur, the parents and the claimants go through the Vaccine Injury Compensation program, as Congress intended.

So I think that strengthening those two components is absolutely critical for keeping manufacturers in the market and also for encouraging other manufacturers to come back into the marketplace.

Senator REED. Dr. Doran?

Dr. DORAN. Senator Reed, on the issue of the NVPO or whatever agency has central responsibility, I think there needs to be a very strong center based at a Federal level that can coordinate this and tease out these problems and bring solutions to the table that we can all agree on.

Senator REED. Thank you both very much, gentlemen.

I would like to thank all the witnesses. Again, we began with a very substantive and very thoughtful report by the GAO, and I want to thank Dr. Heinrich for her excellent testimony.

Thank you, Dr. Doran and Mr. Pisano, for your insights. I am encouraged, actually, that HHS seems to be agreeing with the GAO's recommendations and beginning to implement them. But as you

just pointed out, Dr. Doran, we need a strategy, not just good will and good wishes, and I hope they can develop that strategy quickly.

I hope also that we can move forward on the issue of stockpiling, which seems to be a consensus position of all the witnesses this afternoon. We must play a more active role in Congress to ensure this is done, because we have had hearings before, and we have looked at these issues, and we have a wonderful report, but reports and hearings do not vaccinate children. Consistent, concerted efforts to get them vaccinated, working with providers, manufacturers and the administration will get it done, and we have to get it done.

There has been an impact of these shortages. School entry criteria have been changed. You and your colleagues are working to bring children back into your offices and make sure they have vaccinations that they did not get on time, which comes with a cost. I will be watching closely to ensure that we do not have a lost generation, that we do not have significant numbers of children who have missed their opportunity and did not get a second chance. That would be detrimental to them and also to the public health.

We have made great progress through immunization because of this partnership between the industry, between the Government, and between the medical profession, and we want to continue that partnership and that progress. As I said, one of the great marquis accomplishments of the 20th century has been the vaccination and immunization programs of the United States and of the world. We want to maintain that for the benefit of our children and our grandchildren and generations to come.

Thank you all for an excellent hearing. I will now call the hearing adjourned.

[Additional material follows.]

ADDITIONAL MATERIAL

GAO	<p>United States General Accounting Office</p> <hr/> <p>Testimony</p> <p>Before the Subcommittee on Public Health, Committee on Health, Education, Labor, and Pensions, U.S. Senate</p>
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For Release on Delivery
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CHILDHOOD VACCINES

Challenges in Preventing Future Shortages

Statement of Janet Heinrich
Director, Health Care---Public Health Issues



Mr. Chairman and Members of the Subcommittee:

We are pleased to be here today to discuss recent childhood vaccine shortages. Today we are releasing our report that you, along with seven other Members of the Congress, requested on the subject.¹ My statement today highlights some of the key aspects of our report.

The recent incidents of vaccine shortages began in November 2000 when supplies of the tetanus and diphtheria booster (Td) fell short. By October 2001, the Centers for Disease Control and Prevention (CDC) reported shortages of five vaccines that, because some are combination vaccines, protect against eight childhood diseases. In addition to diphtheria and tetanus vaccines, vaccines to protect against pertussis, invasive pneumococcal disease, measles, mumps, rubella, and varicella were in short supply. In July 2002, updated CDC data indicated supplies were returning to normal for most vaccines. However, the shortage of vaccine to protect against invasive pneumococcal disease was expected to continue through at least late 2002. Concerned about the impact of and reasons for these shortages, you asked that we examine the following questions:

1. To what extent have recent childhood vaccine shortages affected immunization policies and programs?
2. What factors have contributed to the recent shortages, and have they been resolved?
3. What strategies are federal agencies considering to help mitigate disruptions in the vaccine supply?

In brief, shortages have prompted federal authorities to recommend deferring some vaccinations and have caused the majority of states to reduce or suspend immunization requirements for school and day care programs so that children who had received fewer than the previously mandatory immunizations could enroll. States are concerned that failure to be vaccinated at a later date may reduce the share of the population protected and increase the potential for disease to spread; however, data are not currently available to measure these effects.

¹U.S. General Accounting Office, *Childhood Vaccines: Ensuring an Adequate Supply Poses Continuing Challenges*, GAO-02-967 (Washington, D.C.: Sept. 13, 2002).

Multiple factors, including production problems and unanticipated demand for newly approved vaccines, contributed to recent vaccine shortages. While problems leading to the shortages have largely been resolved, the potential exists for shortages to recur. The complex nature and often year-long production schedule of manufacturing a vaccine will continue to make it difficult for the supply system to respond rapidly to sudden changes in supply or demand. Additionally, so few firms make each vaccine (five of the eight recommended childhood vaccines have only one manufacturer each), that production problems or a manufacturer's decision to withdraw may leave few or no alternative sources of vaccine. One development that may increase the supply of vaccines is that a number of new vaccine products that could be used to meet the existing childhood immunization schedule are in varying stages of development. However, completing clinical testing and review by the Food and Drug Administration (FDA) will likely take several years, as these products generally do not qualify for expedited review under FDA policies.

Federal agencies and advisory committees are exploring options to help stabilize the nation's vaccine supply, but few long-term solutions have emerged. Approaches under consideration include strengthening manufacturers' protection against liability for injuries related to childhood vaccines and streamlining the regulatory process. While CDC is considering expanding vaccine stockpiles to provide a cushion in the event of a supply disruption, limited supply and manufacturing capacity will restrict CDC's ability to build them. CDC also lacks a strategy for determining such things as how much vaccine to stockpile, where it should be stored, and how to ensure that the stockpile is additional to a manufacturer's normal inventory. In addition, it is unclear whether the authority that CDC is using to establish these stockpiles provides for their use for all children.

Background

Immunizations are widely considered one of the leading public health achievements of the 20th century. Mandatory immunization programs have eradicated polio and smallpox in the United States and reduced the number of deaths from several childhood diseases, such as measles, to near zero. A consistent supply of many different vaccines is needed to support this effort. CDC currently recommends routine immunizations against 11 childhood diseases: diphtheria, tetanus, pertussis (whooping

cough), *Haemophilus influenzae* type b (most commonly meningitis), hepatitis B, measles, mumps, rubella (German measles), invasive pneumococcal disease, polio, and varicella (chicken pox).³ By combining antigens (the component of a vaccine that triggers an immune response), a single injection of a combination vaccine can protect against multiple diseases.

The federal government, primarily through agencies of the Department of Health and Human Services (HHS), has a role both as a purchaser of vaccines and as a regulator of the industry. The federal government is the largest purchaser of vaccines in the country. CDC negotiates large purchase contracts with manufacturers and makes the vaccines available to public immunization programs under the Vaccines for Children (VFC) program. Under VFC, vaccines are provided for certain children, including those who are eligible for Medicaid or uninsured. Participating public and private health care providers obtain vaccines through VFC at no charge. A second program, established under section 317, of the Public Health Service Act, provides project grants for preventive health services, including immunizations. Currently, CDC supports 64 state, local, and territorial immunization programs (for simplicity, we refer to them as state immunization programs). In total, about 50 percent of all the childhood vaccines administered in the United States each year are obtained by public immunization programs through CDC contracts.

The federal government is also responsible for ensuring the safety of the nation's vaccine supply. FDA regulates the production of vaccines. It licenses all vaccines sold in the United States, requiring clinical trials to demonstrate that vaccines are safe and effective, and reviews the manufacturing process to ensure that vaccines are made consistently in compliance with current good manufacturing practices. Once vaccines are licensed, FDA also conducts periodic inspections of production facilities to ensure that manufacturers maintain compliance with FDA manufacturing requirements.

States also have an important role in immunization efforts. Policies for immunization requirements, including minimum school and day care entry requirements are made almost exclusively at the state level, although cities

³The CDC recommended immunization schedule combines the recommendations approved by the Advisory Committee on Immunization Practices, the American Academy of Pediatrics, and the American Academy of Family Physicians.

occasionally impose additional requirements. Each state also established an immunization infrastructure to monitor infectious disease outbreaks, administer federal immunization grants, manage centralized supplies of vaccine, and otherwise promote immunization policies.

Shortages Prompt Actions to Reduce Immunization Requirements

Recent vaccine shortages have necessitated temporary modifications to the recommended immunization schedule and have caused states to scale back immunization requirements. In our survey of 64 state immunization programs, administered through the Association for State and Territorial Health Officials (ASTHO), all 52 responding programs indicated that they had experienced shortages of two or more vaccines and had taken some form of action to deal with the shortages. Vaccine shortages experienced at the state level have, in turn, prompted cutbacks in immunization requirements for admission to day care or school. Thirty-five states reported putting into effect new, less stringent immunization requirements that allow children who have received fewer than the recommended number of vaccinations to attend school. In general, these states have reduced the immunization requirements for day care and/or school entry or have temporarily suspended enforcement of those requirements until vaccine supplies are replenished. For example, the Minnesota Department of Health suspended the school and postsecondary immunization laws for Td vaccine for the second year in a row, with the suspension extending through the 2002-2003 school year. Other states, including South Carolina and Washington, reported allowing children to attend day care or school even if they were not in compliance with immunization requirements, under the condition that they be recalled for vaccinations when supplies became available.

While it is too early to measure the effect of deferred vaccinations on immunization rates, a number of states reported that vaccine shortages and missed make-up vaccinations may take a toll on coverage and, therefore, increase the potential for infectious disease outbreaks. The full impact of vaccine shortages is difficult to measure for several reasons. For example, none of the national immunization coverage surveys measures vaccination coverage of children under the age of 18 months—the age

cohort receiving the majority of vaccinations.³ While immunization experts generally agree that the residual effects of historically high immunization rates afford temporary protection for underimmunized children, missed immunizations could make susceptible children vulnerable to disease outbreaks. For example, a CDC analysis of a 1998 outbreak of measles in an Anchorage, Alaska, school showed that only 51 percent of the 2,186 children exposed had received the requisite two doses of measles vaccine.

Problems Causing Shortages Largely Resolved, but Shortages Could Recur

No single reason explains the rash of recent vaccine shortages; rather, multiple factors coincided that affected both the supply of and demand for vaccines. We identified four key factors, as follows.

Production Problems - Manufacturing production problems contributed to the shortage of certain vaccines. In some cases, production slowdowns or interruptions occurred when planned maintenance activities took longer than expected; in other cases, production was affected as manufacturers addressed problems identified in FDA inspections. Changes over the last several years in FDA inspection practices may have resulted in the identification of more or different instances of manufacturers' noncompliance with FDA manufacturing requirements. For example, prior to these changes, biologics inspections tended to focus primarily on scientific or technical issues and less on compliance with good manufacturing practices and documentation issues. FDA did take some steps to inform manufacturers about its inspection program changes; however, some manufacturers reported problems related to how well the changes were communicated. FDA issued a compliance program guidance manual detailing the new protocol for conducting inspections intended for FDA staff. However, the information in it could have provided manufacturers a better understanding of the scope of the inspections, but the manual was not made widely available—only upon request.

Removal of Thimerosal - Calls for the removal of the preservative thimerosal from childhood vaccines illustrate the effect that policy changes can have on the supply of vaccine. As a precautionary measure, in

³In August 2002, CDC reported that a limited study in Puerto Rico found a marked decrease in DTap coverage consistent with CDC's recommendation to defer the fourth dose of DTap. See Centers for Disease Control and Prevention, "Impact of Vaccine Shortage on Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Coverage Rates Among Children Aged 24 Months—Puerto Rico, 2002," *Morbidity and Mortality Weekly Report*, vol. 51, no. 30 (2002): 667-668.

July 1999, the American Academy of Pediatrics (AAP) and the U.S. Public Health Service (PHS) issued a joint statement advising that thimerosal in vaccines be eliminated or reduced as soon as possible.⁴ While thimerosal was present in several vaccines, removing it from some vaccines was more complex than for others. For example, one manufacturer of the diphtheria-tetanus-acellular pertussis vaccine (DTaP) had to switch its packaging from multidose to single-dose vials due to the removal of the preservative. This process reduced the manufacturer's output of vaccine by 25 percent, according to the manufacturer.

Manufacturer's Decision to Discontinue Production - Another major factor in the shortage of DTaP, and also Td, was the decision of one manufacturer to discontinue production of all products containing tetanus toxoid. With little advance warning, the company announced in January 2001 that it had ceased production of these vaccines. According to the manufacturer, prior to its decision, it produced approximately one-quarter of all Td and 25 to 30 percent of all DTaP distributed in the United States, so the company's departure from these markets was significant. In the previous year, another manufacturer that supplied a relatively small portion of DTaP also had stopped producing this vaccine. Together these decisions decreased the number of major manufacturers of DTaP from four to two and of Td from two to one.⁵

Unanticipated Demand - The addition of new vaccines to the recommended immunization schedule can also result in shortages if the demand for vaccine outstrips the predicted need and production levels. This was the case with a newly licensed vaccine, pneumococcal conjugate vaccine (PCV), which protects against invasive pneumococcal diseases in young children. PCV was licensed by FDA in February 2000 and formally added to the recommended schedule in January 2001. Company officials said an extensive education campaign prior to its availability resulted in record-breaking initial demand for the vaccine. CDC reported shortages of PCV existed through most of 2001, and the manufacturer was only able to provide about half the needed doses during the first 5 months of 2002.

⁴The joint statement by AAP and PHS also stated that the large risk of not vaccinating children far outweighs the unknown and probably much smaller risk, if any, of cumulative exposure to thimerosal-containing vaccines in the first 6 months of life.

⁵In addition to the one major nationwide supplier of Td, a second manufacturer produces a small amount of Td, primarily for local distribution, and makes some available for nationwide distribution.

Ongoing manufacturing problems limit production, exacerbating the shortage.

While the recent shortages have been largely resolved, the vaccine supply remains vulnerable to any number of disruptions that could occur in the future—including those that contributed to recent shortages and other potential problems, such as a catastrophic plant fire. One key reason is that the nature of vaccine manufacturing prevents the quick production of more vaccine when disruptions occur. Manufacturing a vaccine is a complex, highly controlled process, involving living biological organisms, that can take several months to over a year. Another underlying problem is the limited number of manufacturers—five of the eight recommended childhood vaccines have only one major manufacturer each. Consequently, if there are interruptions in supply or if a manufacturer ceases production, there may be few or no alternative sources of vaccine.

One situation that may help add to the supply of existing vaccines is the development of new vaccines. A recent example is a new formulation of DTaP that recently received FDA approval and has helped ease the shortage of DTaP. We identified 11 vaccines in development that could help meet the current recommended immunization schedule. These vaccines, some of which are already licensed for use in other countries, are in various stages of development, but all must undergo a rather lengthy process of clinical testing and FDA review. While FDA has mechanisms available to shorten the review process, they are not used for most vaccines under development. FDA policies generally restrict the use of its expedited review processes to vaccines that offer protection against diseases for which there are no existing vaccines. Because childhood vaccines under development often involve new forms or combinations of existing vaccines, they typically do not qualify for expedited FDA review.

No Clear Path Yet to Resolve Ongoing Supply Issues

Federal efforts to strengthen the nation's vaccine supply have taken on greater urgency with the recent incidents of shortages. As part of its mandate to study and recommend ways to encourage the availability of safe and effective vaccines, the National Vaccine Advisory Committee formed a work group to explore the issues surrounding vaccine shortages and identify strategies for further consideration by HHS. In its preliminary report, the work group identified several strategies that hold promise, such as streamlining the regulatory process, providing financial incentives for vaccine development, and strengthening manufacturers' liability protection, but it concluded that these strategies needed further study. The work group did express support for expanding CDC vaccine stockpiles

In response to the work group's finding that streamlining the regulatory process needed further study, FDA recently announced that it is examining regulations governing manufacturing processes for both drugs and vaccine products to determine if reform is needed. However, FDA officials told us it is too early to define the scope and time frame for this reexamination. Regarding financial incentives for vaccine development, the Institute of Medicine is currently conducting a study of vaccine pricing and financing strategies that may address this issue.

In regard to liability protections, the work group did make recommendations to strengthen the Vaccine Injury Compensation Program (VICP). VICP is a federal program authorized in 1986 to reduce vaccine manufacturers' liability by compensating individuals for childhood-vaccine-related injuries from a VICP trust fund. The program was established, in part, to help stem the exodus of manufacturers from the vaccine business due to liability concerns. Manufacturers, however, reported a recent resurgence of childhood-vaccine-related lawsuits—including class action lawsuits related to past use of thimerosal—that allege that the lawsuits are not subject to VICP. While the work group acknowledged that recent vaccine shortages do not appear to be related to VICP liability issues, it indicated that strengthening VICP would encourage manufacturers to enter, or remain in, the vaccine production business. Legislation has been introduced for the purpose of clarifying and modifying VICP.⁶

Expansion of Stockpiles Is under Consideration

Also consistent with the work group's recommendations, CDC is considering whether additional vaccine stockpiles will help stabilize the nation's vaccine supply. In 1993, with the establishment of the VFC program, CDC was required to purchase sufficient quantities of pediatric vaccines not only to meet normal usage, but also to provide an additional 6-month supply to meet unanticipated needs. Further, to ensure funding, CDC was authorized to make such purchases in advance of appropriations. Despite this requirement, to date, CDC has established

partial stockpiles for only two—measles-mumps-rubella (MMR) and inactivated polio vaccine (IPV)—of the eight recommended childhood vaccines.

⁶See S. 2053, H.R. 1287, and H.R. 3741.

Even if CDC decides to stockpile additional vaccines, the limited supply and manufacturing capacity will restrict CDC's ability to build certain stockpiles in the near term. CDC estimates it could take 4 to 5 years to build stockpiles for all the currently recommended childhood vaccines—at a cost of \$705 million. Past experience also demonstrates the difficulty of rapidly building stockpiles. Neither the current IPV nor MMR stockpiles have ever achieved target levels because of limited manufacturing capacity. In addition to these challenges, CDC will also need to address issues regarding its authority, strategy, and information needed to use stockpiled vaccines.

Authority - It is uncertain whether stockpiled vaccines purchased with VFC funds can be used for non-VFC-eligible children. While the 1993 legislation required the Secretary of HHS to negotiate for a 6-month stockpile of vaccines to meet unanticipated needs, the legislation did not state that the supply of stockpiled vaccines may be made available for children not otherwise eligible through the VFC program. CDC officials said that the VFC legislation is unclear as to whether stockpiled vaccines can be used for all children.

Strategy - Expanding the number of CDC vaccine stockpiles will require a substantial planning effort—an effort that is not yet complete. For example, CDC has not made key decisions about vaccine stockpiles to ensure their ready release, including the quantity of each vaccine to stockpile, the form of storage, and storage locations. Also, to ensure that use of a stockpile does not disrupt supply to other purchasers, procedures would need to be developed to ensure that stockpiles represent additional quantities to a manufacturer's normal inventory levels.

Information - Once sufficient quantities of vaccines are stockpiled in the appropriate form, CDC needs to make wise decisions on when to deploy the stockpiles. However, CDC currently lacks information for effective decisionmaking. Releasing vaccine from a stockpile in a timely manner requires accurate prediction of a number of variables related to the early identification, severity, and duration of the supply disruption. CDC currently has data that it uses to screen for disruptions in vaccine supply to state immunization programs, but does not have data to anticipate a supply disruption or to fully evaluate the potential severity and duration of a supply disruption, especially to private providers. Through its facility inspections and approvals of production lots, FDA has important information about manufacturers' levels of vaccine production and plant conditions that could affect production. This information could help CDC anticipate supply disruptions and independently assess their potential

severity, but it is only available to CDC by written request. With such information, CDC could set priorities for or resize states' orders and determine how much stockpiled vaccine to release and when to release it. Timely information is important because releasing vaccine from a stockpile can take up to 30 days.

Concluding Observations

The vaccine shortages experienced over the last 2 years demonstrate the vulnerability of the vaccine supply to disruption. Federal agencies are continually challenged to take a proactive approach within their existing missions to help mitigate the effects of these potential future disruptions. Accordingly, our report makes several recommendations to the Secretary of HHS to help promote the availability of vaccine products. These recommendations include adding vaccines to the types of products that can be considered under FDA authority to expedite approval of products in development and directing CDC to address several operational and strategic issues in expanding childhood vaccine stockpiles. The report also contains a matter for congressional consideration to amend the VFC program legislation to address whether vaccines stockpiled under the program are available for use by all children in the event of a shortage.

This concludes my prepared statement, Mr. Chairman. I will be happy to respond to any questions that you or Members of the Subcommittee may have.

Contacts and Acknowledgments

For future contacts regarding this testimony, please call Janet Heinrich, Director, Health Care—Public Health Issues, at (202) 512-7119 or Frank Pasquier at (202) 287-4861. Other individuals who made key contributions include Jennifer Major, Linda McIver, Terry Salki, and Leslie Spangler.



Table 2: Duration of CDC-Reported Childhood Vaccine Shortages

	Vaccine	Approximate start of shortage	Actual or projected end of shortage
In short supply	Tetanus and diphtheria booster (Td)	November 2000	Ended June 2002
	Diphtheria, tetanus, and acellular pertussis (DTaP)	January 2001	Ended June 2002 ^a
	Pneumococcal conjugate vaccine (PCV)	September 2001 ^b	Continue through at least late 2002
	Measles, mumps, and rubella (MMR)	October 2001	Ended June 2002 ^c
	Varicella	October 2001	Ended July 2002
Adequate supply	Hepatitis B (Hep B)		
	<i>Haemophilus influenzae</i> type b (Hib) ^d		
	Inactivated polio vaccine (IPV)		

^aSupplies of DTaP and MMR are sufficient to meet demand for routine use, but not yet sufficient for extensive make-up initiatives.

^bCDC reported shortages of PCV existed throughout most of 2001, but intensified in September 2001.

^cNot considered a shortage by CDC; however, two of three manufacturers reported shipment delays up to 60 days. A third manufacturer had product available.

Source: CDC vaccine shortage reports, July 2002.



American Academy of Pediatrics



TESTIMONY

BEFORE THE

UNITED STATES SENATE

HEALTH, EDUCATION, LABOR AND PENSIONS COMMITTEE

SUBCOMMITTEE ON PUBLIC HEALTH

***"LOSING MOMENTUM: ARE CHILDHOOD VACCINE SUPPLIES
ADEQUATE?"***

**PRESENTED BY:
TIMOTHY F. DORAN, MD, FAAP
CHAIRMAN OF PEDIATRICS
GREATER BALTIMORE MEDICAL CENTER**

**September 17, 2002
2:30 p.m.**

Good afternoon, Mr. Chairman, members of the Committee, I am Dr. Tim Doran, a practicing pediatrician who has taken care of children for almost 20 years. I am also Chairman of Pediatrics at the Greater Baltimore Medical Center, a community hospital in Baltimore, Maryland. On behalf of the American Academy of Pediatrics, I would like to thank you for the opportunity to testify today about the shortage in childhood vaccines that has plagued us over the last year.

The American Academy of Pediatrics (AAP) is an organization of 57,000 primary care pediatricians, pediatric medical subspecialists and pediatric surgical specialists dedicated to the health, safety and well-being of infants, children, adolescents and young adults. My testimony today reflects not only my experiences from my pediatric practice but also those of colleagues from across the United States. As a practicing pediatrician, I would like to share my perspective on the current vaccine shortage, the consequences this has had on vaccine delivery to my patients and their parents, and the impact on my practice.

Overview:

As primary care pediatricians, prevention of disease through immunization is a priority. It is an integral component and major goal of the comprehensive pediatric health care we provide to infants, children, adolescents and young adults. Overall, we deliver approximately 75% of all immunizations. The predictable delivery of safe and effective vaccines is central to our goal of disease prevention.

Immunization is one of the greatest public health achievements of the 20th century and has saved millions of lives. Since the widespread use of vaccines, millions of children have avoided terrible diseases that can cause great suffering and in some cases, death. For example before immunization, polio paralyzed 10,000 - 25,000 children and adults. rubella (German measles) caused birth defects and mental retardation in as many as 20,000 newborns, and measles infected millions of children, killing 400 - 500 and leaving thousands with serious brain damage. Immunizations have reduced by more than 95 to 99 percent the vaccine-preventable infectious diseases in this country.

In the last decade a number of positive changes have occurred in the delivery of vaccines to infants, children and adolescents. Now, in addition to diphtheria and tetanus toxoids and acellular pertussis (DTaP), polio, measles, mumps, rubella (MMR), and Haemophilus

influenza type b (Hib), several new vaccines have been added to the routine vaccination schedule for children, including the hepatitis B vaccine (added in 1994), varicella (chicken pox – introduced in 1995), and the pneumococcal conjugate vaccine (added in 2000).

However, recently, there have been some less than positive changes. In my 22 years of practicing pediatrics, including my pediatric residency training, I have never witnessed a vaccine shortage such as we have seen over the past year. My colleagues and the parents of my patients have been alarmed by the recent and current shortages – remarkable for both the number of different vaccines involved as well as the scarcity of the available supply.

Pediatric Practices:

My office experience has been that the distribution of the required childhood vaccines can be spotty and unpredictable. Over the past year, my practice has seen shortages in several vaccines. These shortages reflect the national disruption of routinely administered vaccines against the eight out of 11 vaccine-preventable childhood infectious diseases. While other vaccines are no longer in short supply the problem remains particularly acute with the new 7-valent pneumococcal conjugate vaccine (PCV7, Prevnar). This vaccine helps protect children from life-threatening meningitis (an infection of the covering of the brain) and blood infections. In fact just last Thursday, I ran out of Prevnar for my practice. Many of my pediatric colleagues, such as those in Wisconsin, are completely out of this vaccine. According to a pediatrician from New Mexico, his high-risk patient population of American Indian/Alaska Native infants currently has no supply of PCV7. This is especially troublesome because this past spring he diagnosed a four-month old Navajo infant with a case of pneumococcal meningitis - a vaccine-preventable childhood infectious disease and as you know American Indian/Alaska Native children are at a far greater risk for life-threatening pneumococcal infections than other children.

Also of concern was the national short supply of the tetanus-diphtheria toxoids (Td) vaccine. Td was in limited supply for over a year and a half. This affected the ability to give teens the booster Td they need. Other vaccines in short supply included DTaP, varicella, and MMR. While the shortage for the Td vaccine is over those adolescents

who did not receive the booster are still at risk because they are one of the most difficult populations to reach in an office visit.

Early this summer, a pediatrician in St. Charles, Missouri called the offices of the American Academy of Pediatrics to describe his serious vaccine shortage problem. He has a small private practice - two pediatricians and one nurse practitioner. He has had difficulty since September 2001 in obtaining both the Prevnar and varicella vaccines. Currently he remains out of Prevnar. Imagine his frustration when he was advised by a patient's mother, who arrived with her son for his one year well-child visit, that she believed her son had been exposed to chicken pox. If he had had any varicella vaccine to offer the patient at that time, research data has found that the child's disease could be ameliorated by vaccination. Just this past Friday we heard a similar story from a solo-practicing pediatrician in a rural community in Oklahoma. His practice does not have Prevnar (he has not had the vaccine since March) but his group-practice colleagues seem to have a supply of the vaccine. He raised the question of why does it appear that there is differential shipping of Prevnar to larger practices?

As you have heard in the past from the Centers for Disease Control and Prevention, several factors contribute to the fragile supply in this country. Vaccine manufacturers are facing increased profitability challenges that force them to re-think their place in the market. For example, the U.S. Food and Drug Administration's Good Manufacturing Practices are being enforced more stringently, which, in some cases, will mean that vaccine makers must build new plants to be in compliance. Some manufacturers have decided it's not worth the investment and have dropped out of the market. For others, poor demand – and thus, poor sales – has been too difficult to surmount, as was the case with the withdrawal from the market of the Lyme vaccine by Smith-Kline-Beecham earlier this year.

Also contributing to the shortages were production issues (including unexpected demand for a vaccine that exceeded supply, in the case of Prevnar), decreased yields of the biologic materials used in certain vaccines, the elimination of some vaccines containing thimerosal as a preservative, and insufficient vaccine stockpiles.

At times I had to explore alternative ways to obtain the full supply of vaccines my practice needs. Sometimes I was more successful obtaining vaccines directly from pharmaceutical representatives than through the bulk purchasing mechanism through the hospital pharmacy. At other times, I borrowed from other practices. There was no opportunity to plan in any reasonable way to anticipate the supply, and unfortunately the pharmaceutical representatives are of little help in predicting when depleted vaccines will become available.

Impact and Consequences:

The real-life impact of these shortages can not be denied. An estimated 11,000 babies are born each day in the United States, each requiring 20 doses of vaccine by age 18 months to be protected against 11 childhood diseases. In addition, there are booster vaccines, such as Td, given in adolescence. A vaccine shortage quickly impacts thousands of families every day.

The parents of my patients have been understandably anxious when they learn that a vaccine is unavailable. They know that there is a small but finite chance that their child might become ill with an otherwise easily-preventable disease because of a delayed or altogether missed vaccine. And many of these diseases, such as measles and meningitis, can be devastating – even fatal – in young children.

Because of negative media coverage on vaccines, I spend a significant amount of time with many parents reassuring them that our vaccines are safe and beneficial. I cannot help but wonder how my credibility, and that of my colleagues, suffers when I then have to explain that these important and safe vaccines are not available for their young child, now at risk for contracting a life-threatening illness. This unduly disrupts the confidence between doctor and parent – a trust that is fundamental to the parent – pediatrician relationship.

Additionally, children who are not vaccinated could possibly be denied entry to school or access to day care. Just recently we saw this occur in Washington, DC. How will school systems deal with increasing numbers of school-age children registering without having completed the vaccination requirements? What will struggling working parents do if their care provider bars their child from day care because he or she is behind on vaccinations?

Moreover, what will parents do when children become unnecessarily sick with vaccine-preventable illnesses that prevent them from attending school or day care and parents miss days from work to care for their sick child?

Along with the stress on the vaccine delivery system and on parents and patients, the vaccine shortage has an administrative impact on my practice as well. We created a system of call-back lists and tickler files to reach those most in need of missed vaccines when they become available. My experience and that of other pediatricians was that these systems are not very reliable or effective. Even in a relatively affluent population, the level of compliance with these call-backs is only fair. The need to effectively track patients and get them back in the office to receive vaccines adds a heavy administrative burden on practices that are already overwhelmed with complex billing issues, referrals, insurance verifications, coding, school and camp forms, medication permissions from schools, prescription refills, phone calls from sick patients, inventory controls, OSHA compliance and documentation, and prolonged holds on the telephone for insurance approvals for certain drugs and procedures.

All this is occurring at a time when the Centers for Medicare and Medicaid Services (CMS) hasn't recognized the physician work associated with the provision of vaccines to patients. This will result in inadequate payment for these services, which will further exacerbate and threaten the already fragile vaccine delivery system. Such lower payments create a disincentive for a pediatrician and other doctors to administer childhood immunizations in a child's "medical home." While there has been some movement and solutions discussed on this issue, it has not been resolved.

Conclusion:

Not only the average practicing pediatrician but also all medical professionals have been issued a wake-up call as we have come to the realization that the vaccine supply, and perhaps the overall vaccine system and infrastructure, is far more fragile than we had imagined. Moreover, this fragility of our nation's vaccine supply, including the integration of new vaccines onto the market is a broad, complex problem, and its solution can only come from the strong leadership and the close involvement of all stakeholders. I believe it is crucial to our children's health that we continue to look for solutions to avoid future

disruptions in supply. I am grateful to have been here today to share my perspective as a practicing pediatrician.

Thank you.

**WAYNE PISANO
EXECUTIVE VICE PRESIDENT
AVENTIS PASTEUR NORTH AMERICA**

**BEFORE THE
SENATE COMMITTEE ON HEALTH, EDUCATION, LABOR AND PENSIONS**

"Losing Momentum: Are Childhood Vaccine Supplies Adequate?"

September 17, 2002

Good afternoon. I'm Wayne Pisano, Executive Vice President of Aventis Pasteur North America. I'd like to thank the committee for providing this opportunity to offer input on issues that are so vital to the health of our nation. We appreciate the time and attention you are devoting to understanding the complexities of the immunization enterprise and to improving it. Aventis Pasteur is one of the world's leading developers and manufacturers of vaccines with U.S. headquarters in Swiftwater, Pennsylvania. Vaccines have been produced at the Swiftwater site since 1897. More than a hundred years later, this campus continues to develop and manufacture vaccines to protect against a variety of diseases in children and adults. We were proud to recently donate to America more than 85 million doses of smallpox vaccine.

Aventis Pasteur is one of the four major global vaccine companies supplying the U.S. Many people are surprised that the industry is so small but that is a direct result of the liability crisis of the 1980's that drove many companies out of the market and about which I will talk later in my testimony.

We are now emerging from an 18-month period in which there have been a number of vaccine shortages. Today, there is ample tetanus vaccine. There is ample DTaP vaccine. It is our understanding that supplies of varicella and MMR vaccines are returning to normal. The fact that the private sector has the capacity to respond reasonably quickly to supply issues demonstrates the strength and vitality of the industry. Having said that, this hearing provides an excellent forum for understanding the underlying causes as well as addressing what can be done to minimize the chances of recurrences and how best to act if there are recurrences. I will offer a number of specific suggestions as to how our nation's vaccine supply can be strengthened while maintaining a vital and productive industry.

1) Impact of Vaccines on Public Health

We have in this country a unique and amazing vaccine enterprise that has resulted in freedom from disease for millions of children. Many of today's parents have never heard of diseases such as polio, *Haemophilus influenza* type b (Hib) or measles, outside of the context of the vaccines that prevent them. Many physicians would be treating some of the tens of thousands of cases of rubella, diphtheria, pertussis and other potential killers if not for our successful efforts. Smallpox has been eradicated. Polio has been eliminated in the U.S. and many other countries with global eradication efforts well underway. Diphtheria, rubella, tetanus, mumps, measles – even Hib disease – are now rarely seen in this country. Since the introduction of a vaccine for Hib little more than a decade ago, the incidence of this disease has plummeted 98 percent in children and is now poised for eradication. Vaccines, in the hands of a robust, cooperative public and private health delivery system, have made these diseases historical artifacts.

This success story is not restricted to the millions of children who receive a vaccine each year. Adults also have benefited enormously from immunization. Approximately 80 million people will receive an influenza vaccine this season; nearly triple the number that did so a decade ago. We fully support the federal government's Healthy People 2010 recommendations to increase immunization against influenza, a disease that still causes 20,000 deaths annually. While the flu vaccine's most important benefit is the number of lives it saves, it also has contributed to reduced incidence and severity of disease, and, as more healthy younger people opt for an annual shot, a payoff to employers in reduced absenteeism and healthcare costs.

With that as background, it is time to take a step back and consider how the immunization enterprise in the country works, what we are doing right and what might be improved.

2) Unique Aspects of the Immunization Enterprise

There are several characteristics of the vaccine enterprise that make the close cooperation of all participants critical for proper alignment of supply with demand. They include the unique nature of vaccines in protecting the public health, the process that recommends and approves them, as well as liability.

First, unlike almost any other aspect of our healthcare system, vaccines protect our entire society in addition to improving personal health. When immunization rates are high, we reduce the incidence of disease even among those who, for medical reasons, cannot obtain protection directly from vaccines. So, there needs to be much closer collaboration during vaccine production, distribution and administration than for other healthcare interventions so that they reflect public health needs. Everyone participating in the immunization enterprise must be involved, be they manufacturers or physicians, nurses or public health workers, policy makers or managed care.

Second, whether or not a vaccine will ever be used widely – or at all – will depend on recommendations formulated through extensive public discussion that incorporates consideration of the production timelines. That collaborative approach has moved mountains over the years.

Third, the regulatory approval process for new vaccines, and for changes to existing vaccines, is highly complex and lengthy with timetables that are difficult to predict. Because production schedules can run as long as 12 months and longer, any abrupt changes in policies that can influence demand for a vaccine or the unanticipated departure of a manufacturer can result in supply interruptions that last for months.

Fourth, as stated earlier, and as some members of this Committee will recall, the liability crisis of the 1980's drove many vaccine manufacturers out of the market. Over a dozen vaccine companies existed prior to 1980. Uncontrollable liability reduced that number to the four that exist today. In 1986, Congress enacted the National Childhood Vaccine Injury Compensation Program (VICP), which helped alleviate some of the liability concerns with a goal of stabilizing liability and the immunization system. That program achieved its initial goals. However, we must now pay renewed attention to the VICP and look at how it can be improved as we once again face a surge in lawsuits with potentially devastating financial exposure.

There are other important factors to consider as well.

Nature of Vaccine Manufacturing

Let's look for a minute at the nature of vaccine manufacturing, which is complex and involves a number of variables that don't exist in pharmaceutical manufacturing. Vaccines require the use of biological organisms, viruses and bacteria, which will not always grow or respond on demand. It is not a matter of opening a tap and pouring out vaccine, no matter who controls the tap. Production lead times are long and the quality control process is the strictest possible. Every lot must pass purity and potency testing, not just by the manufacturer but by the FDA as well. As a result, supply and demand will be misaligned when policy changes increase demand before supply is available. We have experienced several such acute shortages during the past several years; most recently was the DTaP vaccine shortage that began last year. I'll address this in more detail shortly.

Discontinuation of Vaccine Production

The decision by manufacturers to discontinue production of certain vaccines has also been a significant factor in a series of serious but temporary shortages. In the last two years – after a period of relative stability – we have lost production of several vaccines. Companies leave marketplaces when a product no longer provides a reasonable return on investment. Some of the factors that influence return on investment are cost of new product development; cost of manufacturing, which includes escalating investments to meet current good manufacturing practices; product demand; and ability to adjust prices to offset these increasing costs. When a manufacturer discontinues production, ramp up by other manufacturers to fill the gap can take more than a year for some products.

The tetanus shortage we experienced over the last year is a good example. There is now ample tetanus vaccine supply to meet our nation's needs – and because of the investment Aventis Pasteur made in our infrastructure we believe that this supply will be sustained.

Impact of policy changes and regulatory approvals

Policy and regulatory changes also have an enormous impact. I'd like to talk about our experience with two ends of the spectrum and their implications to supply.

Thimerosal

Since mid-1999, several policy making bodies have taken the position that thimerosal should be removed as a preservative from all childhood vaccines. In spite of the fact that there are no reliable scientific data supporting this position, thimerosal is being removed from existing vaccines and withdrawn from consideration as a preservative in new ones. While we don't believe the switch was necessary based on available scientific data, we do support measures that will increase parental confidence and we moved as quickly as possible to that end. However, the policy-making bodies failed to take into consideration the timeline for developing new formulations, securing regulatory approval and producing the new preservative-free vaccines.

The decision to remove thimerosal can serve as a valuable glimpse into the cascade of events that can – and did – create a shortage of a vital childhood vaccine - DTaP. To date, that decision also triggered more than 100 lawsuits against manufacturers, evading the letter and intent of the Vaccine Injury Compensation Program, which you enacted in 1986.

Thimerosal is a preservative that has been used in vaccines for over 50 years. It allows healthcare providers to use convenient multi-dose vials without risking bacterial contamination as they continue to draw from a vial. Without thimerosal, single-dose packaging must be used. In general, manufacturers are able to increase their production capacity when using multi-dose vials rather than single-dose vials. The decision to remove thimerosal had a considerable impact on

supply. For Aventis Pasteur, the manufacturing process had to be changed significantly in order to shift production to single-dose vials. In addition, the process changes lengthened the manufacturers' timelines and yields dropped since it is necessary to overfill every vial to ensure that the provider can remove a full dose. The cumulative effect of this overfill is dramatically greater for single-dose vials than for multi-dose vials. The net impact of these changes was to reduce our supply immediately by 25%.

Reformulating a vaccine, as was required in order to convert from a preservative-containing vaccine to a preservative-free vaccine, requires passage through the regulatory approval process. Any change to a vaccine is a complex endeavor. Manufacturers must take the reformulated product through a license application, with concomitant establishment of new procedures, validation, testing, labeling and getting the product into the marketplace. We invested approximately two years' development effort to replace an existing product.

All vaccine manufacturers strive to supply safe and effective products. However, the point here is that actions have consequences and that those who make the rules need to carefully weigh credible evidence, and must factor in the implications of their decisions on supply and allow realistic time frames when considering such changes. Every independent action has dependent reactions, including some that can be very detrimental.

Return on Investment

Our nation benefits from the efforts of several world-class vaccine companies. At Aventis Pasteur in the U.S., for example, we continue to develop and manufacture improved and new vaccines to protect against a variety of diseases. Over the years, we've had some great successes, including the first application of conjugate vaccine technology and the first infant acellular pertussis vaccine. We have also invested enormous resources into vaccines that, for a variety of reasons, did not reach the marketplace. Although these new product failures do not affect supply directly, the economics do impact the attractiveness of the industry. The full cost of development – contrasted with historical vaccine pricing – is at odds.

The poor return on investment, particularly for older vaccines, has been cited as a cause of supply instability. Historically, vaccine purchasers, including the government, have treated vaccines as commodities, even though they are not, and the system has driven prices down. Raising prices can be difficult, or impossible, yet ongoing investments, often costing millions of dollars, are required to meet evolving Current Good Manufacturing Practices (CGMPs) and to develop improved formulations. It should be no surprise that, when manufacturers find themselves holding low margin products with increasing production costs, they may opt out of the business. In order to ensure that we have state-of-the-art processes and the most modern facilities, manufacturers must be encouraged to invest in infrastructure and allowed to establish an appropriate price and return. Government programs that cap vaccine prices may provide some short-term savings to the federal government, but will have a cost to the long-term stability of the vaccine industry and vaccine supply. A case in point is DTaP vaccine: in the past few years, two of the four manufacturers decided to withdraw from the marketplace.

What Can Be Done to Improve the Immunization Enterprise: A Vaccine Supply Agenda

For the most part, the immunization enterprise is quite efficient. Every child in the United States has access to immunization. No one needs to go without because of cost; both public and private sectors have honed programs over the years that get children to vaccines and vaccines to children. Nearly 20 million routine pediatric visits take place each year, often because immunization is the incentive.

Yet, with what has become nearly universal access, tremendous coverage and added protection, there are still deficiencies in the system that require a tune-up.

Earlier this year, we offered a series of suggestions that we believe would help meet our vaccine supply needs in the future. Some are legislative; others are outside the legislative arena. Our suggestions track closely with the draft recommendations now under review by Secretary Thompson's National Vaccine Advisory Committee made up of the nation's top vaccine experts. We have consulted extensively with GAO during their study of the vaccine supply and in a follow-up to this hearing we will be pleased to provide our comments on the GAO findings.

Let me begin with legislative changes that would help strengthen America's vaccine supply.

LEGISLATIVE CHANGES TO IMPROVE VACCINE SUPPLY

1) Create a Strategic Vaccine Reserve through a long-term commitment to stockpiles.

Vaccines clearly play a strategic role in maintaining the nation's health. It is time that we look to seriously maintain a reserve for both single and multi-source products that is consistent and well funded, allowing government to move quickly to fill the gap should an unexpected shortage occur. Although we have had stockpiles in the past, in recent years the number of vaccines covered and the funding have decreased. To that end, we support additional funding for the CDC to establish stockpiles, as proposed in the Clinton-DeWine bill, which we support for both single and multi-source products. This would effectively create a strategic reserve that would help stabilize supply in the event of temporary shortages.

For example, had there been a tetanus vaccine reserve, the impact from the loss of one manufacturer would have been mitigated and we could have avoided the shortages we recently experienced.

2) Advance notice.

We believe any manufacturer that is voluntarily leaving the market should provide adequate advance notice and we have pledged to do so should that situation ever occur. The obvious exception here is if the withdrawal is involuntary, for example, due to a natural disaster or compliance issue. Earlier this summer, Aventis Pasteur made a public pledge, which we shared with HHS, to provide advance notice should we for any reason discontinue manufacturing any of our vaccines. The Clinton-DeWine legislation addresses this issue as well, however, we do not believe a legislative or regulatory approach would be more effective than a simple voluntary approach. (See attachment A for Aventis Pasteur press announcement of its advance notice proposal.)

We understand that a bipartisan group of Senators on this committee is attempting to shape an appropriate advance notice provision. We look forward to working with you on this issue.

3) Strengthen the Vaccine Injury Compensation Program.

The introduction in 1986 of the Vaccine Injury Compensation Program established a more efficient and user-friendly mechanism for providing financial assistance to families. It also stabilized our national immunization program, reducing the liability uncertainty that had decimated the industry, resulting in a trail of national shortages that led to children going without essential childhood vaccines. The VICP provides a system of compensation and requires that injury claims be litigated initially within it. Recently, new strategies have emerged from vaccine injury claimants intended to circumvent the Program. For those manufacturers who stayed in the industry and worked closely with Congress and others who cared about immunization to enact the original VICP legislation, it is déjà vu. Once again, the industry faces liability exposure in the

billions of dollars, largely because of a significant increase in the number of lawsuits primarily involving vaccines containing thimerosal. We are concerned that, without a re-doubling of the effort needed to address these issues, we will be where we were two decades ago, this time encompassing both pediatric and adult vaccines. We propose strengthening the existing VICP to short-circuit a situation that could have a potentially disastrous impact on public health.

Let me provide an example.

There are now more than 100 lawsuits pending against the four remaining manufacturers alleging the preservative thimerosal as the causative agent of certain neurological disorders. These lawsuits utilize a variety of approaches to try to evade filing claims through VICP. Some of the cases claim that thimerosal is a contaminant and, therefore, is not covered by VICP. Of course, as I stated earlier, thimerosal has been used in vaccines around the world for over 50 years and is in no way a contaminant.

This is a critical area for us. The current legal environment frustrates the intent of VICP, and leaves the immunization enterprise vulnerable to potentially devastating financial liability.

In short, the Frist bill (S. 2053) addresses the massive proliferation of lawsuits by restating more clearly the original intent of the law – i.e., claims against children's vaccines must first go through the compensation program. In addition, Frist improves VICP in ways desired by the claimants by making certain benefits more generous.

Recently, the Advisory Commission on Childhood Vaccines (ACCV), which oversees the VICP and includes trial lawyers, doctors, and parents of injured children, public health officials and manufacturers essentially endorsed the thrust of the Frist bill to bring cases back under the system. We understand Senator Frist has modified his bill to incorporate many of ACCV's changes. We strongly recommend the provisions of the Frist bill to you. Congressmen Greenwood (R-PA) and Towns (D-NY) have introduced companion legislation – H.R. 5282 – in the House.

4) FDA funding in the area of testing research needs to be increased.

The best regulation is knowledgeable regulation and it is essential that CBER have the resources to sustain a state-of-the-art understanding of vaccine testing. This level of expertise is found only in organizations involved in research. Budget cuts in recent years have resulted in a brain drain in this important area.

NON-LEGISLATIVE PROPOSALS

In addition to these legislative initiatives, there are several non-legislative efforts that will improve our nation's vaccine supply.

1) The CDC should be encouraged to act on confidential information to influence supply issues.

The CDC must help the responsible parties effectively address shortages. We previously proposed that the CDC act as a confidential facilitator of critical supply information that is provided by manufacturers, to maintain this data as proprietary and confidential, and also allow it to act upon the information to influence other manufacturers to fill any gap in the event of an imminent shortage. We believe the CDC can act upon such information under its current authority.

2) Strengthen our messages that prevention is the most desirable intervention by providing adequate reimbursement for preventive services.

A reorientation of healthcare priorities to emphasize prevention over cure will provide incentives to doctors to immunize patients and to manufacturers to maintain their commitment to vaccine production.

Our society has traditionally preferred to pay to treat a disease rather than prevent it. People are prepared to spend thousands of dollars a year on a treatment once they contract a disease but will balk at paying modest sums to prevent it from ever happening. If we are to realize the potential of vaccines, we need to change that thinking – and be willing to pay for it.

There needs to be sufficient payment for preventive services. Recent reductions in CMS reimbursement for immunization are disincentives to physicians. Reimbursement rates should reflect the full value of vaccines including a realistic administration fee.

3) Use the expertise of vaccine manufacturers to help formulate sound immunization policy.

Immunization policy will only be as good as the information it's based upon. Manufacturers must have ongoing informational discussions with policymakers and government officials at agencies such as the CDC to provide realistic assessments and expertise about how vaccines are developed and produced, the challenges in doing so, as well as a view into how providers practice and use vaccines. We deal with tens of thousands of providers each year, public and private, cutting across the specialties, and we can share our insights to help improve delivery. It is important that those making vaccine policy, both on staff and on expert committees, have this expertise available to them. However, in more formalized settings, this is no longer occurring. An example is CDC Working Groups where industry representatives are no longer permitted to fully participate in discussions. To exclude industry from these considerations risks that regulations and guidance will be based on incomplete information that could result in wasted resources, inefficient implementation of policy changes and ultimately a loss of faith in our immunization system. We are a resource that should be used. Making policy in a vacuum is a recipe for future supply problems. Industry does not expect to participate in decision-making but, given the limited universe of vaccine expertise, government can benefit from the views of vaccine expertise in industry.

4) Government and advisory bodies need to act with greater predictability.

Continued uninterrupted manufacturing and distribution of vaccines is dependent upon reasonably predictable action by government agencies and advisory committees as well as open lines of communication between those bodies and the manufacturers. Government agencies and advisory committees need to be aware that changes in manufacturing or other regulatory policies could impact future supply, and should take such possibilities into consideration when proposing new policies. Specifically, we suggest that government agencies and advisory committees need to allow adequate advance notice whenever manufacturing changes are necessary. Simply put, if the changes are required before manufacturers can make them and the FDA can approve them, shortages will occur. This happened in the case of thimerosal where the removal schedule was decided on without industry input, resulting in shortages of DTaP. To this end, the regulatory and guideline process needs to be kept predictable, without abrupt changes in requirements of guidelines and with ample opportunity to discuss the implications.

5) Heed the warning signs of a real and present danger – increasing lack of confidence in immunization.

The good news is that parents no longer fear many infectious diseases, because of the success of our immunization programs. Yet, they have also lost respect for the importance of vaccines, as they lack first hand experience or knowledge of the devastating damage vaccine preventable diseases can cause. It would be a failure of immense magnitude if we allow old and conquered scourges to regain a foothold because of misinformation. We urge you to look at ways to bring the public into the process and boost its confidence in immunization. There is as much of an urgent need to address misinformation about immunization as any other aspect of this issue. In a sense, the entire immunization enterprise is under siege.

WHAT WE DON'T NEED

Industry is up to the challenge of producing childhood vaccines that are safe and effective and in sufficient numbers to immunize America's children and adults. In addition, vaccines needed to ensure national security can be obtained from private industry. Case in point is the recent response from industry to NIH's RFP last year for smallpox vaccine.

Several proposals in Congress would undermine incentives for existing and potential manufacturers to produce vaccines. Whether called "national vaccine authority" or "GOCOs" (Government-Owned, Company Operated), each of these proposals results in the federal government getting into the business of manufacturing vaccines.

Government competition would stifle new vaccine entrants into the market without guaranteeing any more supply of vaccines. There are no shortcuts for making vaccines. It is a long and cumbersome process to even create a facility - a process that the government would have to go through before its first dose ever reached the market - probably at least a decade from now. Most important, a GOCO would not have alleviated any of the recent shortages experienced in the U.S.

A GOCO would not result in faster changeover of production lines than would commercial plants in the event of a vaccine shortage, nor would it be able to switch from one vaccine to another since you cannot generally use the same lines for different products without risking cross contamination. This is especially an issue with agents of bioterrorism.

Each vaccine is unique, requiring different features on filling lines. These features would need to be re-standardized and tested for each and every change. No plant could simply be switched to produce influenza or DTaP. Even personnel would be an issue, as different complements of technicians would have to work on different lines given exposure risk issues. A single vaccine exposure problem would cause a ripple of inspections to all lines to prevent cross contamination, stopping production in its tracks. And, even government vaccines would need to show the same standards of safety and efficacy, with all that is incumbent to demonstrate those characteristics.

Science, not manufacturing, is the limiting factor in developing new vaccines. All the manufacturing capacity in the world can't produce a vaccine until science develops the product and the way to make it so that it's safe and effective. Nor do we need new centralized vaccine authorities. The FDA/CDC regulatory regimen is comprehensive and well established.

Additionally, GOCOs or other government subsidized vaccine production and distribution would discourage private sector investment, negatively impacting discovery and innovation.

There is no compelling reason to develop a wholly new system.

The vaccine enterprise in this country is a remarkable success story, I don't believe that it is fragile; yet, it clearly has several areas that can be strengthened. I hope you will give consideration to the proposals we have laid out. Fortunately, we have an industry that wants to partner with government and with all elements of our nation's immunization enterprise to achieve even greater successes.

Thank you again for your attention and your commitment to the immunization system in this country.

Aventis Pasteur



Press Release

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**AVENTIS PASTEUR PLEDGES TO GIVE ADVANCE NOTICE
BEFORE DISCONTINUING VACCINE PRODUCTION**

***Voluntary Commitment Highlights the Importance of Government and Industry
Cooperation***

July 18, 2002 -- SWIFTWATER, PA -- Aventis Pasteur today pledged to provide at least six months advance notice to appropriate government agencies should the company voluntarily cease production of any vaccine, in order to facilitate timely actions to avert supply disruptions. The pledge was contained in a letter from Wayne F. Pisano, executive vice president of Aventis Pasteur North America, to Dr. Eve Slater, assistant secretary for health, U.S. Department of Health and Human Services.

"This move, which is intended to help avert future vaccine shortages, is a reaffirmation of Aventis Pasteur's commitment to be a part of the solution," said Pisano. "We hope other manufacturers will join us in this mission."

In February, Pisano presented a number of recommendations for increasing cooperation between government and vaccine manufacturers to the CDC's National Vaccine Advisory Committee (NVAC) Workshop on Vaccine Supply. During that meeting, he stressed the need for advance notice in order to provide other manufacturers sufficient time to scale up production, which requires substantial planning and investment. Aventis Pasteur became the primary national supplier of the tetanus and diphtheria (Td) vaccine.

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last year when another manufacturer abruptly withdrew from the market causing shortages. Aventis Pasteur recently announced it had increased Td production and is now able to meet the entire nation's needs, leading the CDC to lift its restriction on tetanus immunization.

Other elements of the plan included expanding government stockpiles for use in case supplies are disrupted and requiring government agencies and advisory committees to provide advance notice whenever manufacturing changes are mandated so that companies can make modifications without creating a supply gap.

Last week the company announced it had produced sufficient adult and adolescent vaccine for tetanus and diphtheria to meet the nation's critical care and routine booster needs, prompting the CDC to lift its year-long deferral, enabling physicians to now provide patients with routine Td boosters.

Aventis: A World Leader in Pharmaceuticals

Aventis Pasteur Inc. is located in Swiftwater, PA, and is a subsidiary of Aventis Pasteur SA. Aventis Pasteur Inc. provides the broadest range of human vaccines and biologicals commercially available from any single U.S. vaccine company. It is a leading supplier of vaccines to protect against influenza, diphtheria, tetanus, pertussis, polio, Japanese encephalitis, yellow fever, *Haemophilus influenzae* type b disease, meningitis, rabies, and typhoid fever.

-more-

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Aventis Pasteur, a world leader in vaccines with the broadest range of products, produces more than one billion doses of vaccines every year to immunize 400 million people around the world. Aventis Pasteur, headquartered in Lyon, France, is one of the pharmaceutical activities of Aventis SA.

Aventis (NYSE: AVE) is dedicated to improving life by treating and preventing human disease through the discovery and development of innovative pharmaceutical products. Aventis focuses on prescription drugs for important therapeutic areas such as oncology, cardiology, diabetes and respiratory disorders as well as on human vaccines. In 2001, Aventis generated sales of € 17.7 billion (\$15.5 billion), invested approximately € 3 billion (\$2.6 billion) in research and development and employed approximately 75,000 people in its core business. Aventis corporate headquarters are in Strasbourg, France. For more information, please visit: www.aventis.com

Statements in this news release other than historical information are forward-looking statements subject to risks and uncertainties. Actual results could differ materially depending on factors such as the availability of resources, the timing and effects of regulatory actions, the strength of competition, the outcome of litigation, and the effectiveness of patent protection. Additional information regarding risks and uncertainties is set forth in the current Annual Report on Form 20-F of Aventis on file with the Securities and Exchange Commission.

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[Whereupon, at 3:28 p.m., the committee was adjourned.]

